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PRE-APPEAL BRIEF REQUEST FOR REVIEW

Docket Number (Optional): 107-000110US

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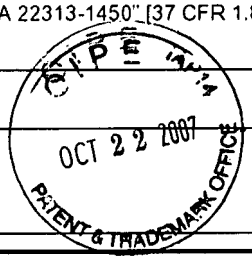
on October 18, 2007

Signature



Typed or printed name Evelyn Gomez

Application Number	Filed
10/044,463	January 10, 2002

First Named Inventor: Davide R. Grassetti

Art Unit	Examiner
1617	Shengjun Wang

Applicant requests review of the final rejection in the above-identified application. No amendments are being filed with this request.

This request is being filed with a notice of appeal.

The review is requested for the reason(s) stated on the attached sheet(s).
Note: No more than five (5) pages may be provided.

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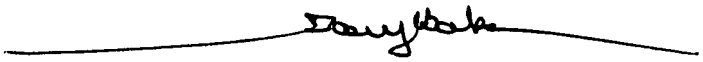

Signature

- [ ] applicant/inventor.
- [ ] assignee of record of the entire interest. See 37 CFR 3.71. Statement under 37 CFR 3.73(b) is enclosed. (Form PTO/SB/96)
- [X] attorney or agent of record. Registration number 41,595
- [ ] attorney or agent acting under 37 CFR 1.34. Registration number if acting under 37 CFR 1.34 _____

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Telephone number

October 18, 2007
Date

NOTE: Signatures of all the inventors or assignees of record of the entire interest or their representative(s) are required. Submit multiple forms if more than one signature is required, see below*.

- [ ] *Total of _____ forms are submitted.

This collection of information is required by 35 U.S.C. 132. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.11, 1.14 and 41.6. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. **SEND TO: Mail Stop AF, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.**

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QUINE INTELLECTUAL PROPERTY LAW GROUP, P.C.

By: _____
Evelyn Gomez

Appl. No.	10/044,463		Confirmation No. 9878
Applicant:	Davide R. Grassetti et al.		
Filed:	January 10, 2002		Docket No.: 107-000110US
TC/A.U.	1617		Customer No.: 22798
Examiner:	Shengjun Wang		

REASONS FOR REVIEW REQUEST

In response to the final Office Action dated May 18, 2007, Applicants herein submit a Request for a Pre-Appeal Brief Conference and an accompanying Notice of Appeal. The Office has cited alleged anticipation as grounds for rejections. Applicant submits that the rejections of record are not proper and without basis, and respectfully request that rejections for alleged anticipation be withdrawn.

A. The § 102 Rejection based on Henderson (U.S. 6,001,555) is improper.

The Final Office Action bases the rejection of claims 23 and 24 on the allegation in section 3 of the Action, that Henderson "discloses the treatment of retroviruses including lentivirus and oncovirus, with disulfides, such as 6,6'-dithiondinicotinic acid." However, this is literally incorrect. Even assuming the statement were correct, it still would not describe the present invention and would not state a *prima facie* case for the rejections.

Claim 23 is directed to, e.g., methods of modulating an immune response in an individual identified in need of a listed immune response by administering, e.g., 6,6'-dithiondinicotinic acid.

Henderson teaches only that "those compounds which inactivate retroviruses, as determined by the methods described herein, can be used to treat retrovirally-mediated diseases...." Emphasis added. However, careful reading of Henderson shows that, e.g., in Table 2 "Disulfide Reagents" 6,6'-dithiondinicotinic acid [CPDS] is not shown to inactivate the virus (see Protein (virus) column associated with abolition of infectivity in the text starting at column 20, line 53). There is a blank space (not tested - see Henderson at column 20, line 55) in the table at the position for data concerning virus inactivation across from the 6,6'-dithiondinicotinic acid (CPDS) entry. Other compounds are offered as inactivating the retrovirus (specifically, HIV) of the assay, but Henderson specifically does not show a determination of CPDS therein to inactivate a virus, and admits it was not tested. Nowhere in Henderson is CPDS determined to inactive a retrovirus. Therefore,

according to the unambiguous statements of Henderson as cited in the Action (column 13, line 51), 6,6'-dithiondinicotinic is indisputably not taught as useful to treat retrovirally-mediated diseases.

The Action further alleges that claims 6 and 7 show "6,6'-dithiondinicotinic acid is particularly claimed as useful against retrovirus." As a preliminary matter, this does not properly allege a teaching of all limitations. In fact, the Henderson claims do not teach all limitations, such as, e.g., identifying an individual in need of immune response modulation, administering a compound to an individual, administering a compound to an individual other than an individual infected with HIV, and modulating one of the specifically listed immune responses.

Claim 6 states, in part:

> 6. A method for inactivating a retrovirus, wherein the retrovirus comprises a structure $Cys(X)_2Cys(X)_4His(X)_4Cys$ which chelates a zinc ion, said method comprising the step of contacting said retrovirus with a compound selected from the group consisting of:
>
> disulfides having the formula R--S--S--R; ...
>
> alpha-halogenated ketones having the formula $X\text{-}CH_2\text{-}CR(=O)$; ...
>
> and wherein R is any atom or molecule, and <u>X is selected from the group consisting of F, I, Br and Cl</u>,
>
> wherein the compound contacts said retrovirus thereby causing dissociation of said zinc ion from said Cys(X)2Cys(X)4His(X)4Cys structure; and
>
> wherein contacting said retrovirus with said compound inactivates said retrovirus.

Applicants note that claim 6 is fatally flawed, or ambiguous at best, for apparently citing a structure of four amino acids halogenated with 10 halogens (i.e., X is F, I, Br or Cl). Applicants believe such a structure does not exist in any retrovirus. If such a structure did exist, Applicants believe it would neither chelate zinc ions, nor would contact with a listed compound necessarily inactivate a retrovirus comprising such a structure. Applicants contend that because the retrovirus of claim 6 does not exist, it can not infect an individual and can not cause the individual to be in need of immune modulation. Claim 6 does not teach anything real or functional, so can not stand as a basis for an allegation of anticipation of any claim.

Assuming arguendo that claim 6 made sense and necessarily taught something functional (and it does not), it still would not anticipate claim 23. The Action alleges claims 6 and 7 show "6,6'-dithiondinicotinic acid is particularly claimed as useful against retrovirus." Even given full scope, the allegation fails to state a *prima facie* case. "Useful against a retrovirus" [not necessarily the HIV of the Henderson inactivation assay] is not "determined by the methods described" in Henderson.

Furthermore, not all members of a Markush group must be functional for the claim to issue, even as not all members of the generic R-S-S-R of claim 6 would function. That is, not all members of the untested wish list claim 7 Markush group would necessarily function to inactivate any retrovirus, and particularly not a real retrovirus (e.g., the HIV used in the Henderson inactivation assay). So additional reasons exist why the Henderson claims can not be said to teach the present claim 23.

In addition, Henderson does not teach the claim 23 limitation of "identifying an individual in need of an immune response, e.g., wherein the individual is other than one infected with HIV. Applicants have noted that not all individuals infected with a retrovirus are necessarily in need immune modulation (to which the present claims are directed), e.g., occult infections with non-pathologic retroviruses (see, e.g., foamy viruses (FVs) or Sharma, M.D., J. Immunology, 1998, 161: 5357-5365) or most retrovirus illnesses, which are known to resolve without modulation of the patient's immune system. Even assuming all retrovirally infected individuals need immunomodulation (and they do not), Henderson still does not teach the limitation of identifying an individual in need, and this is not alleged in the Action. Furthermore, Applicants have noted that the method of Henderson for determination of inactivation by compounds is a method of inactivating HIV in vitro. Scientific conclusions based on this data can only be directed to HIV, at most, and not all retroviruses.

For any number of independent reasons, Henderson can not be said to teach all limitations of independent claim 23 and Applicant respectfully requests the rejections for alleged anticipation be withdrawn.

B. The § 102 Rejection based on Grassetti (U.S. 4,378,364), is improper.

The Examiner has also alleged claims 1, 2, 5, 6, 10 to 12, and 20 to 24 are anticipated by Grassetti '364, which describes treatment of cancer patients with CPDS following surgery to induce a feeling of well-being, pain reduction and increased appetite. The Action acknowledges Grassetti '364 does not teach at least the limitations of immunomodulation or identifying an individual in need of immune response modulation. The Action falls back on "inherency" arguments to allegedly find these limitations not taught by Grassetti '364. References Barber and Tagawa are said to evidence the anticipation and inherency, but Applicant notes they actually teach the aspects of the claims are not inherent in Grassetti '364.

Controlling case law requires that for an aspect to be inherent in prior art, the aspect must necessarily be present in all embodiments. See, e.g., *In re Best*, 195 USPQ 430; *Ex parte Levy*, 17

USPQ2d 1461; and, *Continental Can Co. USA v. Monsanto Co.*, 20 USPQ2d 1746. For example, according to *Continental Can* missing descriptive matter must necessarily be present in the thing described in the reference, or it is not inherent in the reference.

The Action at section 9 states "'identifying an individual in need of immune response modulation;' is inherently met by the method of treating cancer patient disclosed in the reference, as cancer patients are recognized as 'in need of immune response modulation' See, the abstract in Tagawa and columns 1-2 in Barber, et al." However, Applicants have noted that individuals with cancer cells are not necessarily in need of having their immune system modulated. For example, it is known that many cancer cells arise in all of us over the course of our lives and are typically removed by normal unmodulated immune responses and other natural corrective systems, again without the need for modulation of the normal immune response. In many cases, immune response modulation can be toxic or counter-productive. Even the cited references agree that not all cancer patients are in need of immune modulation. For example, Tagawa, in the Action cited abstract, states that modulation of immune responses "is one of the strategies for cancer therapy [not necessarily needed by all patients]. ... However, cytokines may induce toxic reactions or produce no substantial effects ..." Emphasis added. In Figure 1, Tagawa shows how an unmodulated immune system normally works with, e.g., natural antigen presenting cells (APCs) activating cytotoxic T-lymphocytes (CTLs) to provide a normal CTL-mediated unmodulated immune response against a tumor in vivo. This is a clear demonstration that immune modulation is not necessarily needed by cancer patients. With regard to the Barber reference, the citation at columns 1 and 2 makes it clear that cancer patients are not necessarily in need of immune modulation. For example, at column 1, line 35, Barber suggests that 30% of patients treated with surgery alone will have no recurrence. These cancer patents were not treated with immune modulators and did not need them. Chemotheraphies and radiation therapies also have success without resort to immunomodulation. Evidence is extensive that the Action is incorrect in asserting that all cancer patients are necessarily in need of immune modulation, so the allegations do not support the rejections.

Furthermore, at section 9 of the Action, the claim limitation "identifying" is somehow found in the incorrect and insufficient allegation that "cancer patients are recognized as 'in need of immune response modulation." Even if the statement were true, and it is not (as discussed above), it would not demonstrate Grassetti '364 teaching, e.g., identifying an individual in need of an immune response modulation.

Because the references do not teach identifying and actually teach that many cancer patients are not in need of immunomodulation, the inherency required for the rejections does not exist and the rejections should be withdrawn.

C. Summary

Applicants submit that the claims meet the requirements of 35 USC §§112, 102 and 103, being novel, non-obvious and extensively described in the specification. In light of the summary provided herein and the extensive prosecution history, Applicants respectfully request that the rejections be withdrawn and the claims allowed.

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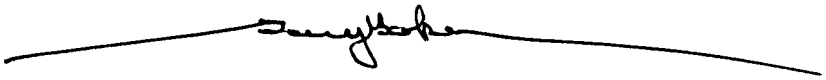
Respectfully submitted,



Gary Baker, J.D., M.T..
Reg. No: 41,595

Attachments: 1) Notice of Appeal; 2) Form PTO/SB/33 (Pre-Appeal Brief Request for Review); 3) petition to extend the period of response for 2 months; 4) A transmittal sheet; 5) fee transmittal sheet; and, 6) receipt indication postcard.